

Coronary Artery to Right Ventricle Fistula in Heart Transplant Recipients: A Complication of Endomyocardial Biopsy

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In a series of 74 heart transplant recipients undergoing annual coronary angiography, a coronary artery to right ventricle fistula was observed in 4 patients, an incidence rate of 5.4%, which is much higher than the expected incidence of congenital coronary artery fistula (0.1% to 0.2%). A traumatic origin of the fistulas is unlikely because none of the heart donors had evidence of chest trauma.

An endomyocardial biopsy-related etiology of the fistulas is postulated. All fistulas were located in the biopsy sampling area. Patients with a fistula underwent more biopsies before the diagnosis compared with patients without a fistula (20 ± 11 versus 14 ± 6 , $p = 0.05$). At least one large arteriole (diameter >0.16 mm) was found on pathologic examination of the biopsy specimens from each of the

patients with a fistula (100%) but in only 2 (16.7%) ($p < 0.01$) of 12 randomly selected patients without a fistula. The size of the fistula appears to be hemodynamically insignificant in all four patients, judging from angiographic size, normal intracardiac pressures and normal cardiac output values at rest.

The diagnosis of a coronary artery to right ventricle fistula is possible and should be entertained at the time of coronary angiography of heart transplant recipients. The clinical significance of the finding is unclear. As long as endomyocardial biopsy remains the diagnostic method of identifying tissue rejection, prevention of the described complication is unlikely.

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Transvenous right ventricular endomyocardial biopsy remains the standard method for diagnosis of tissue rejection in heart transplant recipients. The technique and instrumentation for percutaneous access through the internal jugular vein was developed by Caves et al. (1). A method using femoral venous access was described in 1984 (2). The feasibility and safety of serial outpatient biopsies were also documented (3).

The reported complication rate of post-transplant biopsies is low: 0.3% (4 of 1,300 procedures) in the Stanford experience (4) and 0.4% (24 of 6,200 procedures) in the Hartfield Hospital series (5). Major complications include right ventricular perforation and complications related to central vein cannulation (pneumothorax and air embolism).

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Transient arrhythmias, transient right bundle branch block, transient nerve palsies (Horner's, recurrent laryngeal and phrenic) and prolonged puncture site bleeding are considered minor complications. In this report, we present four cases of coronary artery to right ventricle fistula as a newly recognized complication of endomyocardial biopsy in heart transplant recipients.

Methods

Included in this study were all 74 patients who underwent cardiac transplantation at the University of Alabama at Birmingham between November 1981 and December 1986 and who also underwent at least one annual diagnostic cardiac catheterization for early detection of obstructive coronary artery disease and for diagnosis of asymptomatic allograft rejection.

Right ventricular biopsy. The annual study included right and left heart catheterization, coronary arteriography and endomyocardial biopsy. Right heart catheterization preceded left heart catheterization. A 7F Swan-Ganz thermodilution catheter was used to obtain intracardiac pressures and

to determine cardiac output at rest. Right ventricular biopsy was performed by the internal jugular venous route with use of the Standard reusable biptome (Scholten Surgical Instruments) (90% of cases) or by the femoral venous route with use of the Cordis disposable biptome (Cordis Corporation) (10% of cases).

The technique of endomyocardial biopsy used was similar to previously published methods (2,4). Briefly, for the internal jugular vein approach, the Scholten biptome was advanced under fluoroscopic control (anteroposterior projection) into the right atrium with the tip pointing laterally. The instrument was then advanced after counterclockwise rotation into the right ventricle and the tip was pointed toward the interventricular septum (the handle clamp was pointed posteriorly). The presence of induced premature ventricular contractions served as an indicator of contact with endocardium (as opposed to inadvertent cannulation of the coronary sinus). The properly placed biptome was gently withdrawn about 1 cm, the jaws were opened and the instrument was re-advanced toward the endocardium; the jaws were closed and the tissue sample was obtained with a tug.

In the femoral vein approach, the right femoral vein was entered with use of the Seldinger technique; a long radiopaque sheath was introduced into the right ventricle and flushed and the disposable Cordis biptome was placed against the right intraventricular septum. The proper placement of the instrument was verified, if there was doubt, in the left anterior oblique projection. The tissue samples were obtained with use of a technique similar to that described for the Scholten biptome. Four to five myocardial tissue samples were obtained during each procedure. The estimated average sample size was 3 to 5 mm in the longest diameter.

Selective left and right coronary angiography was performed by the Judkins technique (6). Change in shunt size on follow-up angiograms was estimated visually and by measuring the diameter of the feeding artery.

The total number of all biopsies performed in each patient was noted as well as the number of biopsies performed before the first annual coronary angiogram. A nonpaired *t* test was used to test for difference between the number of biopsies performed in the groups with and without an arteriovenous shunt. The cause of death of the heart donors was obtained from the Organ Bank records.

Histopathologic study. All pathologic slides of four patients with a coronary artery fistula (80 biopsies) and all slides of 12 randomly selected transplant patients without a coronary artery fistula (178 biopsies) were reviewed for presence of large arterioles in the myocardial biopsy specimen. Vessel diameter (D) was estimated from measured vessel circumference (C): $D = C/3.14$ (mm). Large arterioles (Fig. 1) were defined as vessels with a diameter >0.16 mm (or circumference >0.5 mm).

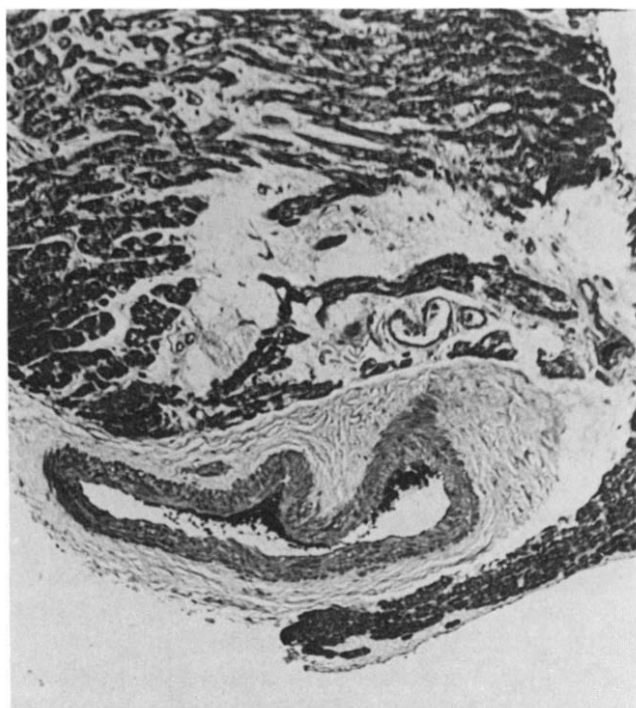


Figure 1. Example of a large arteriole in the endomyocardial biopsy specimen.

Results

In 4 of the 74 heart transplant recipients (5.4%; confidence limit 2.7% to 8.1%) a coronary artery to right ventricle fistula was observed during the 1st annual angiographic evaluation. None of these four patients had a heart murmur.

Case Reports (Table 1)

Case 1. A 51 year old woman with end-stage ischemic cardiomyopathy received a heart from a 23 year old male donor who died of closed head trauma without evidence of

Table 1. Hemodynamic and Oximetric Data in Four Cases at the Time of Fistula Detection and Number of Biopsies Performed Before Fistula Detection

Case No.	Pressures (mm Hg)					No. of Biopsies Before Fistula Detection
	RA	RV	PA	PCW	CI	
1	5	21/6	21/11	6	2.9	8
2	4	32/5	28/12	10	3.3	15
3	3 (72)*	27/2 (73)*	32/15 (74)*	7	3.6	24
4	2	20/2	24/12	8	3.0	33

*Numbers in parentheses indicate percent of oxygen saturation. CI = cardiac index (liters/min per m^2); PA = pulmonary artery (systolic/end-diastolic); PCW = pulmonary capillary wedge; RA = mean right atrial; RV = right ventricular (systolic/end-diastolic).

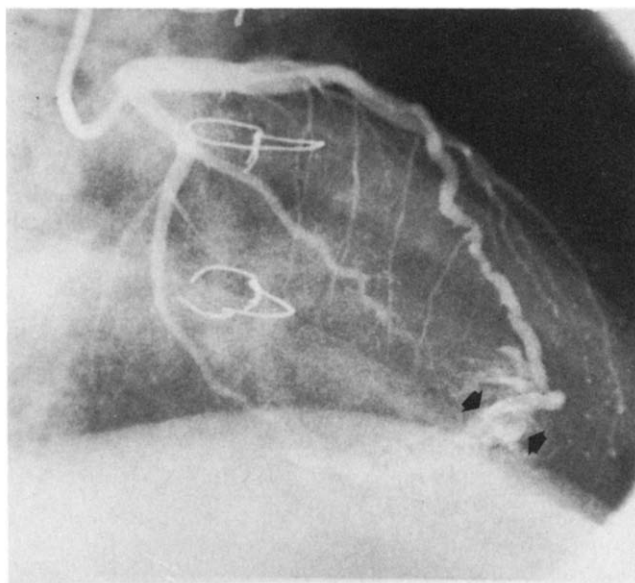


Figure 2. Case 3. Left anterior descending coronary artery to right ventricle fistula (arrows).

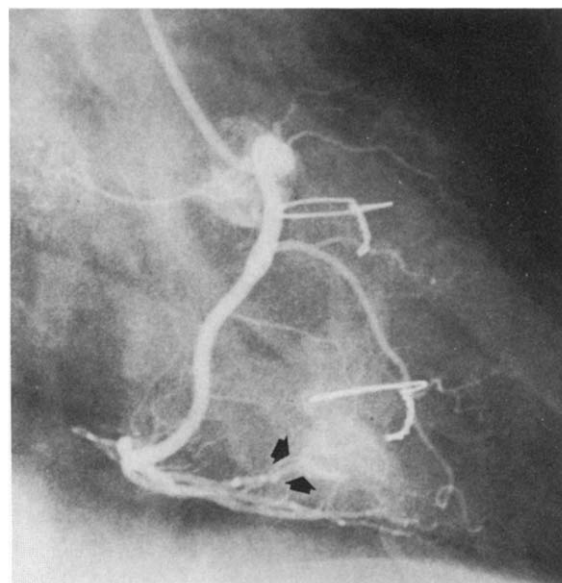


Figure 3. Case 4. Fistula from the right ventricular branch of the right coronary artery to the right ventricle (arrows).

chest contusion. Her 1st annual coronary angiogram revealed a communication between the septal branch of the left anterior descending artery and the right ventricular cavity. The size of the shunt was small, appeared unchanged between the 1st and the 2nd year studies, but was larger and multiple on the 3rd year study. A new fistula between a right ventricular marginal branch of the right coronary artery and the right ventricle was detected in the 3rd year study.

Case 2. A 44 year old woman with end-stage ischemic cardiomyopathy received a heart from a 19 year old male donor who died of head trauma without evidence of chest trauma. Communications between the septal branch of the anterior descending coronary artery as well as the right ventricular branch of the right coronary artery and the right ventricular cavity were detected 1 year after the transplant. The size of both shunts appeared unchanged on the second annual angiogram.

Case 3. A 58 year old man with end-stage ischemic cardiomyopathy received a heart from a 22 year old male donor who died of a gunshot wound to the head. One year after the transplantation, a fistula between the distal third of the left anterior descending coronary artery and the right ventricular cavity was diagnosed (Fig. 2). The feeding artery was tortuous and dilated. Right heart oximetry performed 4 months later demonstrated no step-up in blood oxygen saturation (Table 1).

Case 4. A 48 year old white man with end-stage cardiomyopathy received a heart from a 33 year old male donor who died of head trauma sustained by a fall; only superficial abrasions on the chest were noted. The 1st annual coronary angiogram revealed a fistula between the right ventricular

branch of the right coronary artery and the right ventricular cavity (Fig. 3). The fistula was smaller on the 2nd annual angiogram.

Etiology Postbiopsy Fistula

Role of frequency of biopsy. The 70 patients without an arteriovenous communication underwent 14 ± 6 biopsies (range 6 to 29) before the 1st annual coronary angiogram, whereas the 4 patients with a fistula underwent 20 ± 11 (range 18 to 33) biopsies during the 1st post-transplant year ($p = 0.05$). During the whole observation period (24.6 ± 13.5 months) the total number of biopsies in patients without a fistula was 19 ± 7 (range 9 to 40), which is no different from the number of biopsies performed in patients with a fistula before the diagnosis (20 ± 11 , range 18 to 33) ($p = 0.70$). The shunt was detected in all four patients at the time of the 1st annual study.

At least one large arteriole was found in the myocardial biopsy specimen of all 4 patients with a coronary artery fistula (100%) but in only 2 (16.7%) of the random sample of 12 patients without a fistula ($p < 0.01$). Three of the four fistulas detected involved a right ventricular branch of the right coronary artery and may have resulted from a biopsy of the right ventricular free wall or the right ventricular apex.

Other biopsy-related complications. In our series of 74 transplant patients, 1,397 endomyocardial biopsies were performed during the period encompassed by this report. Overall, procedure-related complications were infrequent and included the following: sustained supraventricular tachycardia (two patients), sustained ventricular tachycardia

(one patient), bronchospasm possibly related to intravenous antibiotics (two patients), internal jugular vein thrombosis (one patient), pleuritic pain after biopsy with small pericardial effusion on echocardiogram (one patient) (no drainage was required).

Discussion

This report describes four cases of coronary artery to right ventricle fistula in heart transplant recipients and provides data to demonstrate that fistula formation is a rare complication of endomyocardial biopsy. The incidence rate of the coronary artery fistulas in this patient population was 5.4% (4 of 74 patients), >25 times the 0.2% incidence rate (101 of 55,856 patients) of congenital coronary artery fistulas reported from routine coronary angiograms at the Cleveland Clinic ($p < 0.0001$). Only 4 (0.007%) of those 101 fistulas drained into the right ventricle (7). Gillebert et al. (8) reported 20 fistulas (19 congenital, 1 traumatic) among 14,708 patients, an incidence rate of 0.1%, compared with our 5.4% ($p < 0.001$). Only two fistulas in their series (0.01%) drained into the right ventricle.

Etiology of fistulas. An endomyocardial biopsy-related etiology of coronary artery fistulas in our patients is suggested by the frequency and location of the communications and the new appearance of the fistula on the 3rd annual angiogram (Case 1). A traumatic origin of the fistulas seems unlikely because all four donors in our series died of head trauma without evidence of chest trauma. Of 25 traumatic coronary artery fistulas previously reported (9), 20 (80%) were caused by penetrating chest trauma.

Clinical significance. The hemodynamic significance of arteriovenous fistulas after endomyocardial biopsy is most likely negligible, considering their small angiographic size, normal intracardiac pressures and cardiac index at rest and negative oximetric findings in Case 3 (Table 1).

From our experience, it appears that routine biopsies can be performed after a fistula has been identified. It is currently unclear in which patient the fistula will progress in size with increased shunting (9) or will spontaneously regress (10). It would seem prudent, however, to direct future biopsies away from the area of a known fistula. Although not seen in this experience, a potential must exist for the development of bacterial endocarditis in the presence of a jet lesion, irrespective of the size of the shunt (11).

From our observations we infer that the combination of more frequent endomyocardial biopsies during the 1st post-transplant year and the presence of large arterioles in the area of biopsy may predispose to the development of coronary artery to right ventricle fistula. Inadvertent right ventricular free wall biopsy in the distribution of right coronary artery branches may also contribute to fistula development.

Addendum

Since submission of our report, two series of coronary artery to right ventricle fistula were reported: 1) a 14% incidence rate (in 5 of 35 patients) in the McGill University experience (Fitchet et al., *Am J Cardiol* 1988;62:829-31); and 2) an 8% incidence (in 14 of 176 patients) at the University of Pittsburgh (Sandhu et al., *Circulation* 1989;79:350-6).

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